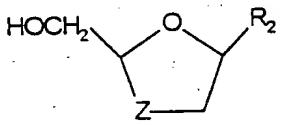
CLAIMS:

~~1. A process for preparing an oxathiolane of formula~~ (I), pharmaceutically acceptable salts or esters, and geometric and optical isomers thereof:

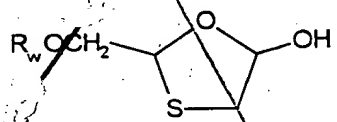


(I)

wherein:

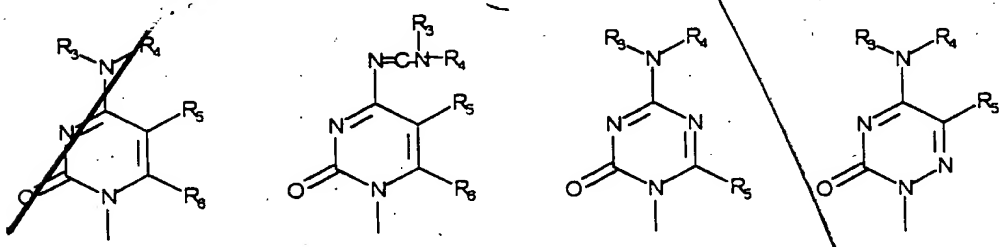
R_2 is a purine or pyrimidine base or an analogue or derivative thereof; and Z is S, S=O or SO_2;

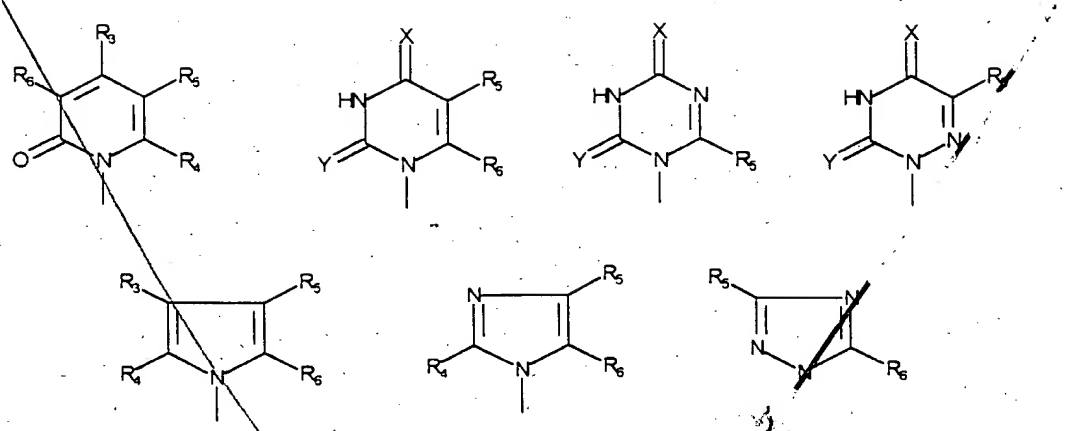
-the process comprising the step of reacting a mercaptoacetaldehyde with a compound having formula R_wOCH_2CHO, wherein R_w is hydrogen or a hydroxyl protecting group R_1,
under neutral or basic conditions to obtain an intermediate of formula (XIII):



(XIII)

2. The process according to claim 1, wherein in formula (I), R_2 is selected from the group consisting of:





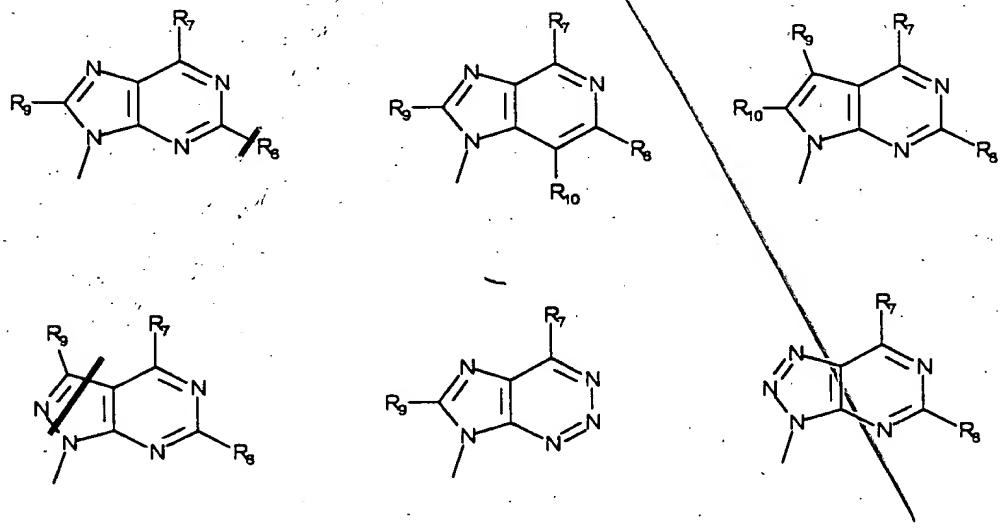
wherein:

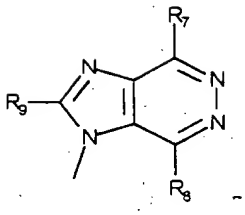
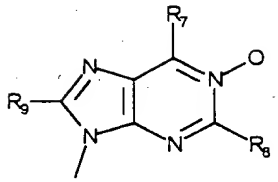
X is oxygen or sulfur; Y is oxygen or sulfur;

R_3 and R_4 are independently selected from the group consisting of hydrogen, hydroxyl, amino, substituted or unsubstituted C_{1-6} alkyl, or C_{1-6} alkenyl or C_{1-6} alkynyl, and substituted or unsubstituted C_{1-10} acyl or aracyl;

R_5 and R_6 are independently selected from the group consisting of hydrogen, halogen, hydroxyl, amino, cyano, carboxy, carbamoyl, alkoxycarbonyl, hydroxymethyl, trifluoromethyl, thioaryl, substituted or unsubstituted C_{1-6} alkyl or C_{1-6} alkenyl or C_{1-6} alkynyl, and substituted or unsubstituted C_{1-10} acyloxy;

and



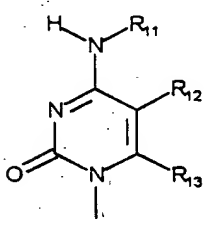
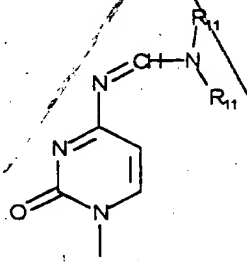
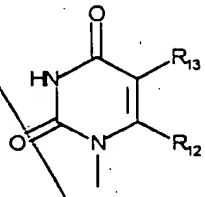
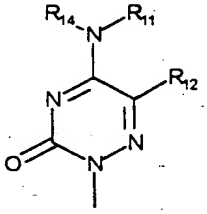
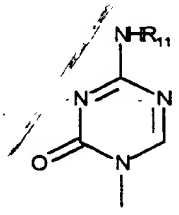
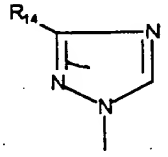
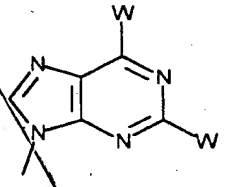



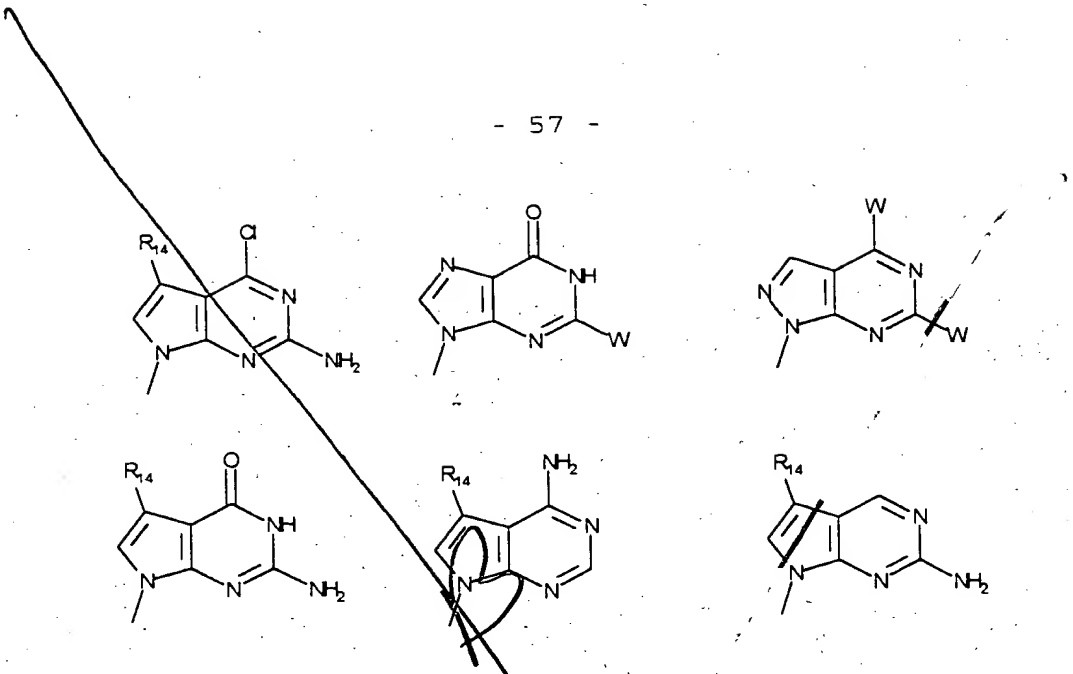
wherein:

R_7 and R_8 are independently selected from the group consisting of hydrogen, hydroxy, alkoxy, thiol, thioalkyl, amino, substituted amino, halogen, cyano, carboxy, alkoxycarbonyl, carbamoyl, substituted or unsubstituted C_{1-6} alkyl, or alkenyl, or alkynyl, and substituted or unsubstituted C_{1-10} acyloxy; and

R_9 and R_{10} are independently selected from the group consisting of hydrogen, hydroxy, alkoxy, amino, substituted amino, halogen, azido, substituted or unsubstituted C_{1-6} alkyl or alkenyl or alkynyl, and substituted or unsubstituted C_{1-10} acyloxy.

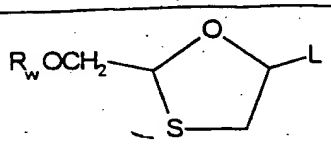
3. The process according to claim 1, wherein R_2 is selected from the group consisting of:



wherein each R_{11} is independently selected from hydrogen, acetyl, and C_{1-6} alkyl groups;
R_{12} and R_{13} are independently selected from hydrogen, hydroxymethyl, trifluoromethyl, substituted or unsubstituted C_{1-6} alkyl or alkenyl, bromine, chlorine, fluorine, and iodine;
R_{14} is selected from hydrogen, cyano, carboxy, ethoxycarbonyl, carbamoyl, and thiocarbamoyl; and
each W is independently selected from hydrogen, bromine, chlorine, fluorine, iodine, amino, and hydroxyl groups.

4. The process according to claim 1, 2 or 3, wherein the hydroxyl of the intermediate of formula (XIII) is converted to a suitable leaving function L to obtain an intermediate of formula (XIV):



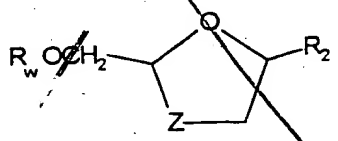
(XIV)

wherein, R_w is hydrogen or R_1, wherein R_1 is a hydroxy protecting group, and L is a leaving group.

5. The process according to claim 4, wherein L is OR_z, wherein R_z is selected from the group consisting of:

hydrogen, a substituted or unsubstituted saturated or unsaturated alkyl group, a substituted or unsubstituted aliphatic or aromatic acyl group, a substituted or unsubstituted saturated or unsaturated alkoxy carbonyl group, a substituted or unsubstituted sulphonyl imidazolide, a substituted or unsubstituted carbonyl imidazolide, a substituted or unsubstituted aliphatic or aromatic amino carbonyl group, a substituted or unsubstituted alkyl imidate group, a substituted or unsubstituted saturated or unsaturated phosphinoyl, and a substituted or unsubstituted aliphatic or aromatic sulphonyl group.

6. The process according to claim 4, further comprising the step of reacting the intermediate of formula (XIV) with a silylated pyrimidine or purine base or an analogue thereof, in the presence of a Lewis acid to produce a compound of the formula (IX):



(IX)

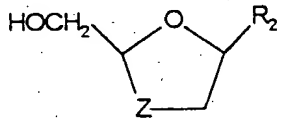
wherein R_2 and R_w have the same meaning as in claim 4, and Z is S.

7. The process according to claim 6, wherein the sulfur of the intermediate of formula (IX) may optionally be oxidized to give an intermediate of formula (IX) wherein Z is S=O or SO_2.

8. The process according to claim 1, 2 or 3, wherein the mercaptoacetaldehyde is obtained from a mercaptoacetaldehyde dimer dissolved in an inert solvent.

~~9. The process according to claim 8, wherein the inert~~ solvent is selected from the group consisting of: pyridine, toluene and DMSO.

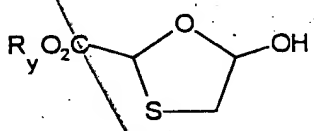
10. A process for preparing an oxathiolane of formula (I), pharmaceutically acceptable salts or esters, and geometric isomers thereof, and mixtures of those isomers:



(I)

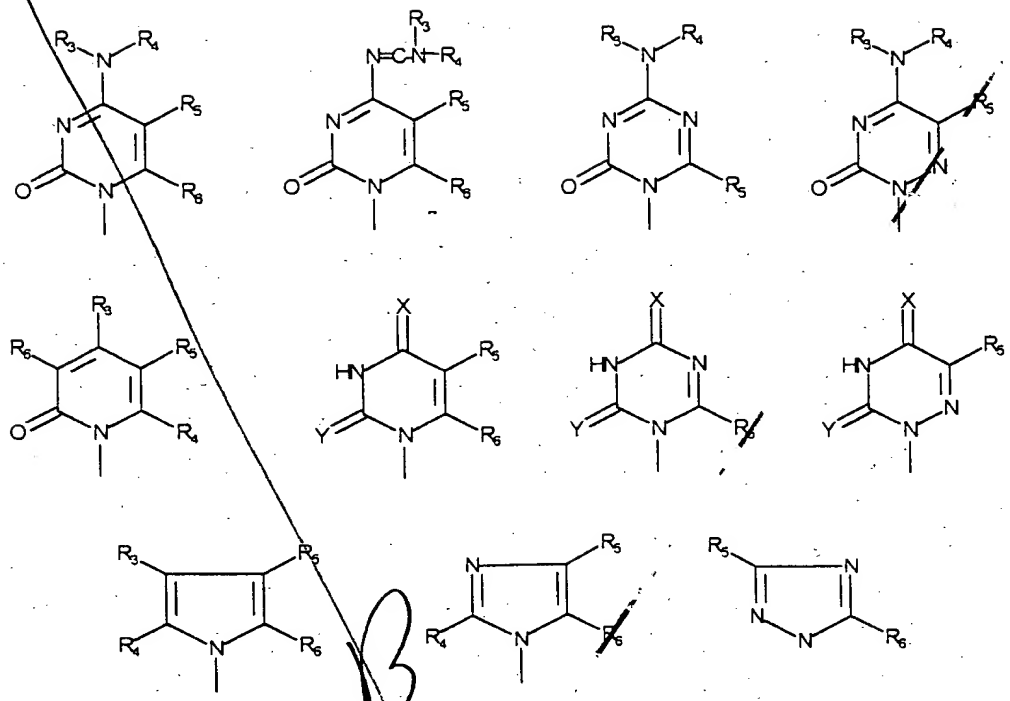
wherein:
R_2 is a purine or pyrimidine base or an analogue or derivative thereof; and
Z is selected from a group consisting of S, S=O and SO_2;

-the process comprising the step of reacting a mercaptoacetaldehyde with a compound having formula $R_yOOCCHO$, wherein R_y is substituted or unsubstituted C_{1-12} alkyl or substituted or unsubstituted C_{6-20} aryl to obtain an intermediate of formula (XV):



(XV)

11. The process according to claim 10, wherein, in the formula (I), R_2 is selected from the group consisting of:



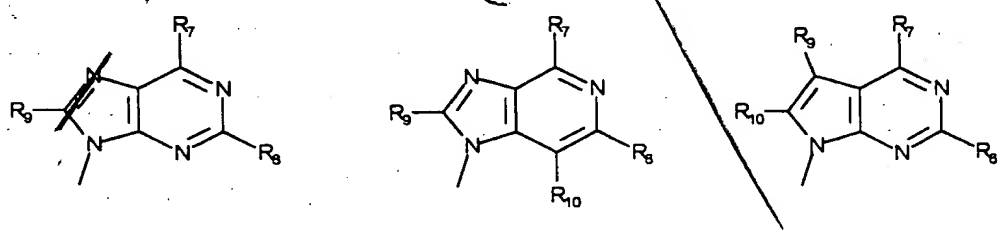
wherein:

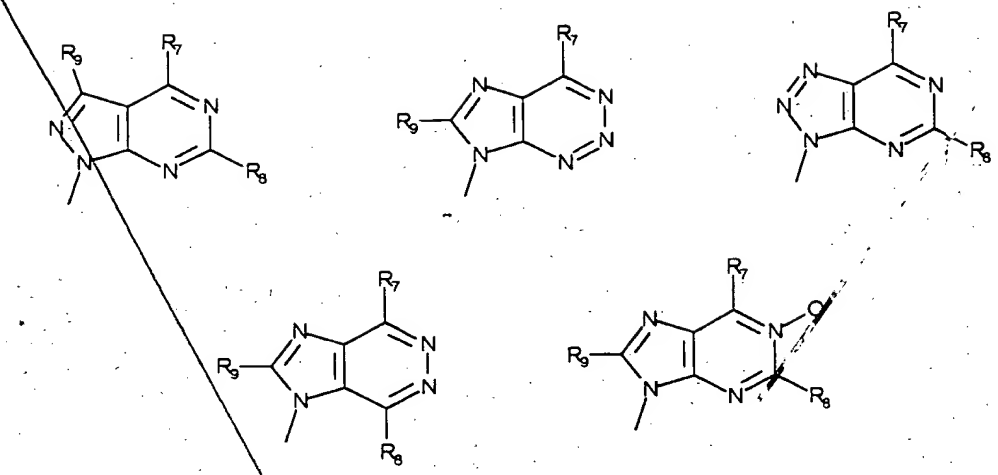
X is oxygen or sulfur; Y is oxygen or sulfur;

R_3 and R_4 are independently selected from the group consisting of hydrogen, hydroxyl, amino, substituted or unsubstituted C_{1-6} alkyl, or C_{1-6} alkenyl or C_{1-6} alkynyl, and substituted or unsubstituted C_{1-10} acyl or aracyl;

R_5 and R_6 are independently selected from the group consisting of hydrogen, halogen, hydroxyl, amino, cyano, carboxy, carbamoyl, alkoxycarbonyl, hydroxymethyl, trifluoromethyl, thioaryl, substituted or unsubstituted C_{1-6} alkyl or C_{1-6} alkenyl or C_{1-6} alkynyl, and substituted or unsubstituted C_{1-10} acyloxy;

and



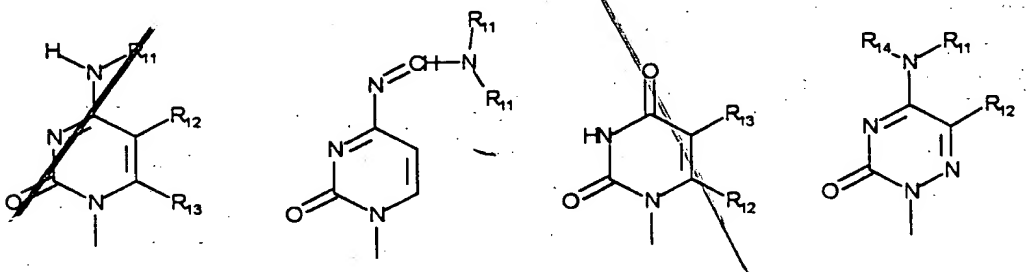


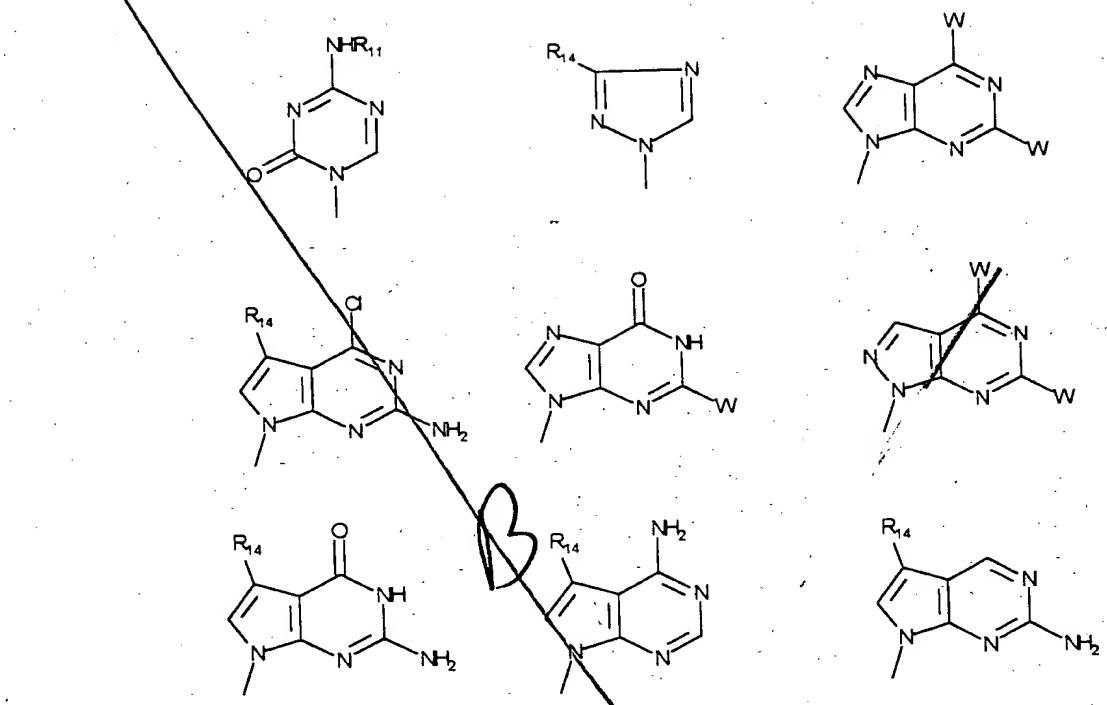
wherein:

R_7 and R_8 are independently selected from the group consisting of hydrogen, hydroxy, alkoxy, thiol, thioalkyl, amino, substituted amino, halogen, cyano, carboxy, alkoxycarbonyl, carbamoyl, substituted or unsubstituted C_{1-6} alkyl, or alkenyl, or alkynyl, and substituted or unsubstituted C_{1-10} acyloxy; and

R_9 and R_{10} are independently selected from the group consisting of hydrogen, hydroxy, alkoxy, amino, substituted amino, halogen, azido, substituted or unsubstituted C_{1-6} alkyl or alkenyl or alkynyl, and substituted or unsubstituted C_{1-10} acyloxy.

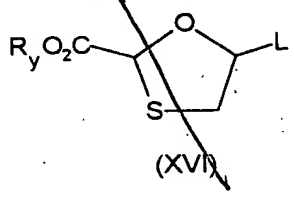
12. The process according to claim 10, wherein R_2 is selected from the group consisting of:





wherein each R_{11} is independently selected from hydrogen, acetyl, and C_{1-6} alkyl groups;
R_{12} and R_{13} are independently selected from hydrogen, hydroxymethyl, trifluoromethyl, substituted or unsubstituted C_{1-6} alkyl or alkenyl, bromine, chlorine, fluorine, and iodine;
R_{14} is selected from hydrogen, cyano, carboxy, ethoxycarbonyl, carbamoyl, and thiocarbamoyl; and
each W is independently selected from hydrogen, bromine, chlorine, fluorine, iodine, amino, and hydroxyl groups.

13. The process according to claim 10, 11 or 12, further comprising the step of converting the hydroxyl of the intermediate of formula (XV) to a suitable leaving function L to obtain an intermediate of formula (XVI):

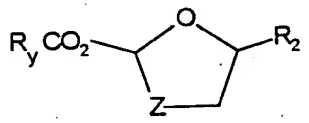


(XVI)

wherein R_y is as defined in claim 10, and L is a leaving group.

14. The process according to claim 13, wherein L is OR_z, wherein R_z is selected from the group consisting of: hydrogen, a substituted or unsubstituted saturated or unsaturated alkyl group, a substituted or unsubstituted aliphatic or aromatic acyl group, a substituted or unsubstituted saturated or unsaturated alkoxy carbonyl group, a substituted or unsubstituted sulphonyl imidazolide, a substituted or unsubstituted carbonyl imidazolide, a substituted or unsubstituted aliphatic or aromatic amino carbonyl group, a substituted or unsubstituted alkyl imidate group, a substituted or unsubstituted saturated or unsaturated phosphinoyl, and a substituted or unsubstituted aliphatic or aromatic sulphonyl group.

15. The process according to claim 13 or 14, further comprising the step of reacting the intermediate of formula (XVI) with a silylated base or an analogue thereof, in the presence of a Lewis acid to produce a compound of formula (XVII):

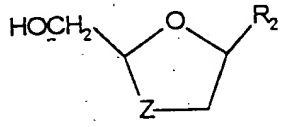


(XVII)

wherein Z is S, and R_y has the same meaning as in claim 13, and R_2 is a purine or pyrimidine base, an analogue or derivative thereof.

16. The process according to claim 15, wherein the sulfur of the intermediate of formula (XVII) may optionally be oxidized to give an intermediate of ~~formula (XVII) wherein Z is S=O or SO_2.~~

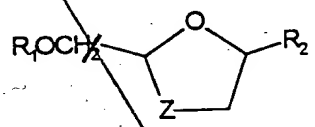
~~17. The process according to claim 16, further~~ comprising the step of reducing the intermediate of formula (XVII) to a compound of formula (I):



(I)

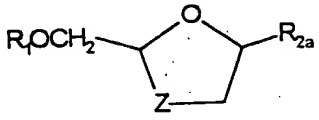
wherein:
R_2 is a purine or pyrimidine base or an analogue or derivative thereof; and
Z is selected from a group consisting of S, S=O and SO_2.

18. The process according to claim 17, further comprising the steps of:
(a) protecting the hydroxyl group of the compound of formula (I) with a suitable protecting function R_1 to obtain an intermediate of formula (XIX):



(XIX)

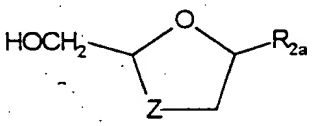
wherein R_1 is selected from the group consisting of: C_{1-16} acyl, t-butyldimethylsilyl, and t-butyldiphenylsilyl;
(b) interconverting the purine or pyrimidine base substituent or analogue thereof R_2 of formula (XIX) to another pyrimidine or purine base or analogue thereof R_{2a} to obtain an intermediate of formula (XX):



(XX)

and

(c) removing the protecting function R_1 of the intermediate of formula (XX) to obtain a compound of formula (I):



(I)

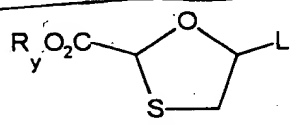
wherein Z is as defined in claim 13.

19. The process according to claim 10, 11 or 12, wherein the mercaptoacetaldehyde is obtained from a mercaptoacetaldehyde dimer dissolved in an inert solvent.

20. The process according to claim 19, wherein the inert solvent is selected from the group consisting of: pyridine, toluene, and DMSO.

21. The process according to claim 10, 11 or 12, further comprising the steps of:

(a) converting the hydroxyl of the intermediate of formula (XV) to a suitable leaving function L to obtain an intermediate of formula (XXI):

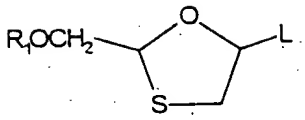


(XXI)

wherein R_y is substituted or unsubstituted C_{1-12} alkyl or substituted or unsubstituted C_{6-20} aryl;

(b) converting the carboxyl to a hydroxymethyl function; and

(c) protecting the resulting hydroxymethyl with a suitable protecting function R_1 to obtain an intermediate of formula (XXII):

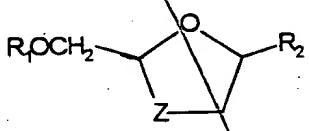


(XXII)

wherein R_1 is selected from the group consisting of: C_{1-16} acyl, t-butyldimethylsilyl, and t-butyldiphenylsilyl.

22. The process according to claim 21, wherein L is OR_z, wherein R_z is selected from the group consisting of: hydrogen, a substituted or unsubstituted saturated or unsaturated alkyl group, a substituted or unsubstituted aliphatic or aromatic acyl group, a substituted or unsubstituted saturated or unsaturated alkoxy carbonyl group, a substituted or unsubstituted sulphonyl imidazolide, a substituted or unsubstituted carbonyl imidazolide, a substituted or unsubstituted aliphatic or aromatic amino carbonyl group, a substituted or unsubstituted alkyl imidate group, a substituted or unsubstituted saturated or unsaturated phosphinoyl, and a substituted or unsubstituted aliphatic or aromatic sulphonyl group.

23. The process according to claim 21, further comprising the step of reacting the intermediate of formula (XXII) with a silylated pyrimidine or purine base or an analogue thereof, in the presence of a Lewis acid to obtain an intermediate of formula (XXIII):

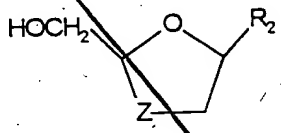


(XXIII)

wherein R_1 is as defined in claim 21, R_2 is a purine or pyrimidine base, analogue or derivative thereof, and Z is S.

~~24. The process according to claim 23, wherein the~~ intermediate of formula (XXIII) is optionally oxidized to obtain an intermediate of formula (XXIII) wherein Z is S=O or SO_2.

25. The process according to claim 24, further comprising the step of removing the hydroxyl protecting function R_1 from compound (XXIII) to obtain a compound of formula (I):



(I)

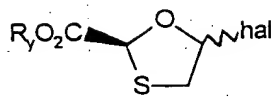
wherein Z is S, S=O, or SO_2, and R_2 is a purine or pyrimidine base or an analogue or derivative thereof.

26. The process according to claim 6, wherein the Lewis acid is selected from the group consisting of: TMSOTf, TMSI, $TiCl_4$, and $SnCl_4$.

27. The process according to claim 15, wherein the Lewis acid is selected from the group consisting of: TMSOTf, TMSI, $TiCl_4$, and $SnCl_4$.

28. The process according to claim 23, wherein the Lewis acid is selected from the group consisting of: TMSOTf, TMSI, $TiCl_4$, and $SnCl_4$.

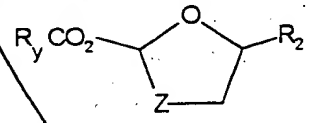
29. The process according to claim 13, further comprising the steps of:
a) reacting the intermediate of formula (XVI) with a halogen-containing silyl Lewis acid to obtain an intermediate of formula (XXVI):



(XXVI)

wherein hal is halogen, and

b) coupling the intermediate of formula (XXVI) with a base or analogue thereof R_2 under basic conditions, to obtain an intermediate of formula (XVII):



(XVII)

30. The process according to claim 29, wherein said halogen is iodine.

31. The process according to claim 29, wherein said Lewis acid is TMSI.

32. The process according to claim 29, 30 or 31, wherein the R_2 base or analogue thereof is a purine.

33. The process according to claim 32, wherein the purine is 6-chloropurine.

34. Intermediates useful for the production of oxathiolane compounds, said intermediates selected from the group consisting of:
trans-2-hydroxymethyl-5-acetoxy-1,3-oxathiolane;
cis-2-benzoyloxymethyl-5-hydroxy-1,3-oxathiolane,
trans-2-benzoyloxymethyl-5-hydroxy-1,3-oxathiolane and mixtures thereof;
cis-2-benzoyloxymethyl-5-(4',5'-dichlorobenzoyloxy)-1,3-oxathiolane, *trans*-2-benzoyloxymethyl-5-(4',5'-dichlorobenzoyloxy)-1,3-oxathiolane and mixtures thereof;

cis-2-benzoyloxymethyl-5-trimethylacetoxy-1,3-oxathiolane, *trans*-2-benzoyloxymethyl-5-trimethylacetoxy-1,3-oxathiolane and mixtures thereof; *cis*-2-benzoyloxymethyl-5-(2',2',2'-trichloroethoxycarbonyloxy)1,3-oxathiolane, *trans*-2-benzoyloxymethyl-5-(2',2',2'-trichloroethoxy carbonyloxy)1,3-oxathiolane and mixtures thereof; *cis*-2-benzoyloxymethyl-5-ethoxycarbonyloxy-1,3-oxathiolane, *trans*-2-benzoyloxymethyl-5-ethoxycarbonyloxy-1,3-oxathiolane and mixtures thereof; *cis*-2-benzoyloxymethyl-5-methoxycarbonyloxy-1,3-oxathiolane, *trans*-2-benzoyloxymethyl-5-methoxycarbonyloxy-1,3-oxathiolane and mixtures thereof; *cis*-2-benzoyloxymethyl-5-acetoxy-1,3-oxathiolane, *trans*-2-benzoyloxymethyl-5-acetoxy-1,3-oxathiolane and mixtures thereof; *cis*-2-benzoyloxymethyl-5-(N4'-acetylcytosin-1'-yl)-1,3-oxathiolane, *trans*-2-benzoyloxymethyl-5-(N4'-acetylcytosin-1'-yl)-1,3-oxathiolane and mixtures thereof; *cis*-2-benzoyloxymethyl-5-(cytosin-1'-yl)-1,3-oxathiolane, *trans*-2-benzoyloxymethyl-5-(cytosin-1'-yl)-1,3-oxathiolane and mixtures thereof; *cis*-2-carboethoxy-5-hydroxy-1,3-oxathiolane, *trans*-2-carboethoxy-5-hydroxy-1,3-oxathiolane and mixtures thereof; *cis*-2-carboethoxy-5-methoxycarbonyloxy-1,3-oxathiolane, *trans*-2-carboethoxy-5-methoxycarbonyloxy-1,3-oxathiolane and mixtures thereof; *cis*-2-carboethoxy-5-acetoxy-1,3-oxathiolane, *trans*-2-carboethoxy-5-acetoxy-1,3-oxathiolane and mixtures thereof; *cis*-2-carboethoxy-5-(N4'-acetylcytosin-1'-yl)-1,3-oxathiolane; *cis*-2-carboethoxy-5-(cytosin-1'-yl)-1,3-oxathiolane; *cis*-2-carboethoxy-5-(uracil-1'-yl)-1,3-oxathiolane;

cis-2-benzoyloxymethyl-5-(cytosin-1'-yl)-1,3-oxathiolane;
cis-ethyl-5-iodo-1,3-oxathiolan-2-carboxylate, *trans*-ethyl-5-iodo-1,3-oxathiolan-2-carboxylate and mixtures thereof;
cis-ethyl-5-(6'-chloropurin-9'-yl)-1,3-oxathiolan-2-carboxylate, *trans*-ethyl-5-(6'-chloropurin-9'-yl)-1,3-oxathiolan-2-carboxylate and mixtures thereof; and
cis-ethyl-5-(6'-chloropurin-7'-yl)-1,3-oxathiolan-2-carboxylate, *trans*-ethyl-5-(6'-chloropurin-7'-yl)-1,3-oxathiolan-2-carboxylate and mixtures thereof.

add B1